



PATENT
Attorney Docket No.3.0-008

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

Villafane et al

Serial No.:09/653,717

Filed: September 1, 2000

For: Use of Nicotine or
Derivative thereof for the
Treatment of Neurologic
Diseases, in particular
Parkinson Disease

)
)
) Group Art Unit: 1614

)
) Examiner: R. Cook

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FEB 27 2004

DECLARATION PURSUANT TO 37 C.F.R. § 1.132

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

I, Gabriel Salvadore VILLAFANE do hereby state and declare the following:

1. I am a co-inventor of the subject matter disclosed and claimed in the above-captioned application. I have ten (10) years of experience working in the field of Neurology. My Curriculum Vitae is attached as Exhibit 1.

2. I have reviewed the latest Official Action mailed September 16, 2003. It appears to me that in this Official Action the Examiner deems that the above-captioned patent application is obvious in the absence of unexpected results. We have obtained results and have observed them in patients which were administered with 0.2 mg to 5 mg per day per kilogram of body weight of nicotine and L-DOPA in a dose at least 30% lower than the effective dose when L-DOPA is administered in the absence of nicotine.

3. The patients chosen for this study had the following characteristics. The patients have had Parkinson Disease for a period of about 5 to 12 years. All of the patients chosen for this study were non smokers. Their ages ranged from 48 to 65 and the patients were previously treated with a classical treatment of L-DOPA, in addition to other classical medications. Neurological examination of these patients showed classical Parkinson Disease symptoms including severe motor, vegetative and cognitive symptoms. They presented at least some of the classical symptoms of Parkinson Disease which are bilateral akinesia, rigidity, arm tremors, gait and speech disturbances, masked faces, urological problems, sebaceous excess on the skin and disorganized thinking. Clinical evaluation of the patients having Parkinson's disease was carried out using conventional UPDRS I, II and III neurological tests. UPDRS stands for Unified Parkinson's Disease Rating Scale. A patient who has Parkinson's Disease has a UPDRS average of 42 without treatment. The observed results were compared with the UPDRS scale which is the following :

- UPDRS results between 0-17 corresponded to a normal neuro-psychological behavior;
- UPDRS results between 17-32 relates to neuro-psychological symptoms of Parkinson's Disease;
- UPDRS results superior to 32 corresponds to the Parkinson's Disease.

During the classical treatment with L-DOPA, patients have a meanUPDRS average of 24. Nevertheless, after about 5 years with L-DOPA treatment, secondary effects, like dyskinesia, increase drastically and Parkinsonian symptoms reappear.

4. The patients in paragraph 3 were administered nicotine at month 2 transdermally at a rate of from 0.2 mg to 5 mg per day per kilogram of body weight and a reduced in a dose at least 30% lower than the effective dose when L-DOPA is administered alone. The amount of nicotine administered increased over the next three consecutive months and stabilized at month 5 to month 8. From month 8 to month 24, the nicotine dosage that was administered was gradually increased.

5. The observed results were the following. Partial improvement of all symptoms was observed in the majority of patients three (3) months after beginning of the treatment with nicotine. At month 5 individual UPDRS III "Off" score improved

from 42 to 33 (33/42), arm tremor was reduced (0/3) rigidity (0/2) gait (0/2) and speech (0/2) were all reduced. UDPRS I (mental state) changed significantly (0/10) and UDPRS II (daily life, on-off) improved in both "off" (10/22) and "on" (6/3) scores. After 6 months, a major improvement in daily life activities was observed by others. For example, one patient undertook working in the garden, cycling and swimming after treatment at 6 months, while these activities were suspended for several years before. In addition handwriting was improved, speech was clearer, vocal volume was stronger and expression of emotions was restored. Improvement in urinary and sexual functions, as well as mood and memory was observed. Furthermore, stabilization of the orthostatic blood pressure was also observed. After 24 months of treatment as set forth in paragraph 4, the following was observed in the patients. Complete disappearance for the first time of dystonia and dyskinesia. Cognitive function was improved, as well as antiretrograde and retrograde memory problems. Axial symptoms associated with Parkinson's Disease such as voice articulation, phonation, walking equilibrium and turning right and left were also improved. Urological symptoms improved to such a degree that urological consultations were suspended. The skin quality was less sebaceous.

6. Besides the above study, another study was undertaken using functional imaging of the dopamine transporter (DAT), which defines the integrity of the dopaminergic system. 6 patients having Parkinson's Disease at stage IV of Hoehn and Yahr that were previously administered the classical treatment of L-DOPA (see, paragraph 7 below) were given a control DaTScan prior to the administering the treatment set forth in paragraph 4 above for only 8 months. After 8 months the DaTScan was repeated and revealed an increase of D1 and D2 pre-synaptic dopaminergic receptors in the nigrostriatum zone and thus a restructuration of this area. The DaTScan was administered as follows: first of all, the patients received potassium iodide orally to block the thyroid before intravenous injection of 153MBq [123 I]-FP-CIT (DaTScan, Amersham Health, FR); second, the brain SPECT (Single Photon Emission Computed Tomography) was performed 3 hours later using a dual-head camera, equipped with high-resolution collimators, in 128 x 128 matrices and for a total imaging time of 45 minutes. Quantification of striatal uptake was performed by means of circular regions of interest, drawn over the caudate nucleus, putamen

and occipital cortex. The ratio of specific striatal uptake to non displaceable uptake was calculated as an estimate of the dopamine receptor binding potential (BP).

7. The classical procedure used for Parkinson's disease patients is the administration of levodopa (L-DOPA). L-DOPA was introduced into clinical practice around 1967 and its administration was seen to be effective in improving akinesia and postural disorders in about 75% of patients, but its administration rarely improves rest tremor. Pharmacologically, L-DOPA is known to increase dopamine levels in the striatum and restores neurotransmitter balance between dopamine and acetylcholine. Nowadays, L-DOPA is often given in combination with a carboxylase inhibitor (carbidopa) which prevents destruction of L-DOPA in the bloodstream and peripheral tissues. Generally, a total dosage of L-DOPA from 300 mg to 2000 mg daily is administered to patients having Parkinson's disease. The dosage is progressively increased in accordance with the stage of the Parkinson's disease. The administration of L-DOPA, however does not address the underlying problem associated with Parkinson's disease, but only relieves some of the symptoms associated with this disease. Presently all patients diagnosed with Parkinson's disease will eventually require L-DOPA treatment.

8. The first side effects of patients treated with L-DOPA and/or L-DOPA and carbidopa are nausea, vomiting, abdominal pain, anxiety, agitation, difficulty in speaking, memory loss, distress, numbness, delusions, hallucinations, insomnia, orthostatic hypotension and sometimes arrhythmia. The major difficulties experienced by patients using this classical therapy over time include fluctuations or sudden variations in response to the drugs used, known as "on-off response", the development of akinesia (weakness or immobility) and dyskinesia/dystonia (difficulty in performing voluntary movements), which are very problematic as Parkinson's disease progresses. One-third to one-half of patients on the classical L-DOPA therapy experience progressive dementia, as well as visual and tactile hallucinations.

9. As set forth in paragraph 6 above, the classical treatment using L-DOPA did not show any improvement in an increase of D1 and D2 pre-synaptic dopaminergic receptors in the nigrostriatum zone and thus a restructuration of this area. Hence, this treatment does not have an effect on the underlying disease of Parkinson's.

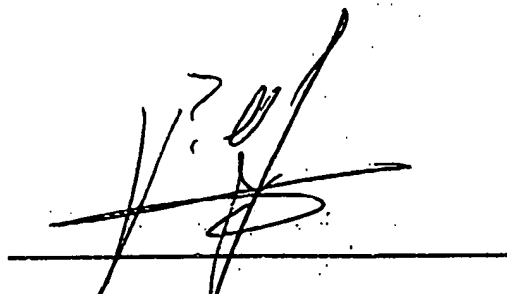
10. The Domino et al reference teaches that 12.5 mg/kg, a dose chosen since it provided effective relief of symptoms of Parkinson's disease when given alone, with various doses of nicotine. Although not noted in this reference, certainly some of the side effects as set forth in paragraph 8 above occurred in this monkey model, due to the dose of L-DOPA. If the same amount of L-DOPA (12.5 mg/kg) was administered to patients with Parkinson's disease, the side effects would be similar to those in paragraph 8.

11. In conclusion, it is observed that patients having Parkinson's disease, which were administered 0.2 mg to 5 mg per day per kilogram of body weight of nicotine and L-DOPA in a dose at least 30% lower than the effective dose when L-DOPA is administered in the absence of nicotine have improved symptoms such as a reduction in arm tremor, rigidity, gait and speech and an improvement in urinary and sexual functions, as well as mood and memory, in comparison with the classical treatment with L-DOPA. Moreover, an improvement of dopaminergic transporters at level of the striation, i.e., an improvement of dopamine uptake by D1 and D2 receptors was demonstrated using the treatment in the above-captioned patent application, while side effects of dyskinesia and akinesia were either totally abolished or improved.

12. I further declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

16/02/2004

Date



Gabriel Salvador VILLAFANE



CURRICULUM VITAE

Gabriel Salvador VILLAFANE

Date of Birth : December 21, 1961 in Cordoba (Argentina)

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Doctor of medicine (1987)

Qualification in Neurology (1990)

SUPERIOR STUDIES

Certificate so obtained

Assistant appointed to the chair of philosophy in the catholic university of Cordoba
(01.03.1982 to 30.11.1982)

Assistant appointed to the chair of philosophy in the catholic university of Cordoba
(01.03.1983 to 03.08.1984)

Assistant in the haematology department of Hospital Italiano.

Doctor of medicine (September 10, 1987)

Qualification in Neurology (02.08.1987 to 09.09.1990) in the public hospital of
Cordoba (Department of Health Hospital San Roque - Cordoba - Argentina)
delivered by Dr. A.M. Lopez de Cardeilhac, responsible of the Neurology Department
and Dr. S.M. Foglia the Hospital Director.

Foreign Doctor of Medicine of Paris Hospitals (31/10/1992)

ERUDITE SOCIETY

Member of the French Society of Neurology

TITLES AND HOSPITAL ACTIVITIES

May 1987	Medical Assistant in the Neurology Department of Hospital San Roque
Jan.1988 to Nov.1988	Doctor in the Urgency Department of Hospital San Roque
Oct.1987 to Oct.1988	medical Assistant in the Clinical and Medical Department of Hospital San Roque
June 1989 to Dec.1989	Doctor in the Urgency Department of Hospital San Roque
1991-1992	Intern in the Neurology Department of Hospital Mondor (Pr. J-D Degos)

Since 1992	Team member of the Research on cerebral transplant in Parkinson's disease managed by Pr Cesaro – Neurology Department of Hospital Mondor
Since 1992	Full-time neurologist in the Neurology department (Pr. Degos) of Hospital Mondor
Since 1993	Weekly consultations in the Neurology Department (Pr. Degos) of Hospital Mondor
Since 1992-1996	Neurologist in the Neurology Department (Pr. Degos) of Hospital Mondor (Senior neurologist in the urgency Department)
Since 1995-1999	Part-time neurologist in the Medical and Nutrition Department (Pr. Jacotot) of Hospital Mondor
Since 1998	Full-time neurologist in the Neurology Department (pr. Louarn) of Hospital Albert Chenevier

PUBLICATIONS

P1 : Long-term outcome of unilaterally transplanted parkinsonian patients. I. Clinical approach.
G.Defer, C.Geny, F.Ricolfi, G.Fenelon, J-C Montfort, P.Remy, G.Villafane, R.Jeny, Y.Samson, Y.Keravel, A.Gaston, J-D.Degos, M.Peschanski, P.Cesaro, J-P.Nguyen.
Brain (1996) 119,41-50.

P2 : Speech improvement in a parkinsonian patient after bilateral mesencephalic intra-striatal graft.
G.Villafane, G.Defer, J-P.Nguyen, P.Brugierres, J-C.Montfort, P.Remy, R.Jeny, J-D.Degos, M.Peschanski, P.Cesaro.
Subjected

COMMUNICATIONS

C1 : Unilateral foetal grafting in 5 parkinsonian patients
G.defer, J-Pngyuen, G.Fenelon, C.Geny, F.Ricolfi, J-C.Montfort, P.Remy, Y.Samson, G.Villafane, P.Hantraye, R.Jeny, A.Gaston, Y.Keravel, J-D.Degos, M.Peschanski, P.Cesaro
Communication to the Caen's meeting of the French Society of Neurology, October 14, 1994.

C2 : Unilateral foetal grafting in Parkinson's Disease : clinical results after 18 to 36 months of follow-up.
G.Defer, G.Fenelon, J-P.Nguyen, C.Geny, F.Ricolfi, G.Villafane, J-C.Montfort, P.Remy, Y.Samson, P.Hantraye, R.Jeny, A.Gaston, Y.Keravel, J-D.Degos, M.Peschanski, P.Cesaro.
Third Lille Neurosciences Workshop, October 20-21, 1994.

C3 : Speech improvement in a parkinsonian patient after bilateral mesencephalic intra-striatal graft.

P.Cesaro, G.Defer, J-P.Ngyuen, P.Brigieres, J-C.Montfort, P.Remy, G.Villafane,
R.Jeny, J-D.Degos, M.Peschanski.

6th International neuronal transplantation meeting, San Diego, February 1996.

C4 : Long-term nicotine treatment in Parkinson'disease : report of 2 cases.

G.Villafane, J-D.Degos, G.Lagrue, S.Petras, P.Cesaro.

6th International Congress of parkinson's disease and movement disorders,
Barcelone, June 2000.

C5 : Lon-term nicotine treatment in Parkinson'disease : report of cases after two
years.

G.Villafane

XIV International Congress of Parkinson's Disease, Helsinki, Finland, July 28-31
2001.

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fashioned refer to something dating from the past. **ancient** implies existence or first occurrence in a distant past: *an ancient custom*. **antiquated** connotes something too old or no longer useful: *an antiquated building*. **antique** suggests a curious or pleasing quality in something old: *antique furniture*. **old-fashioned** may disparage something as being out of date or may approve something old as being superior: *an old-fashioned hat*; *old-fashioned courtesy*. — **Ant.** 2. new.

ancient² (än'shənt), *n.* Obs. 1. the bearer of a flag. 2. a flag, banner, or standard; ensign. [var. of **ENSIGN** by confusion with **ANCIENT**]

ancient Arabic Order of the Nobles of the Mystic Shrine. See under **Shrine**.

ancient history, 1. the study or a course of study of history before the end of the Western Roman Empire A.D. 476. 2. *Informal*. Information or events of the recent past which are common knowledge or are no longer pertinent: *Last week's news is ancient history*.

anciently (än'shənt lē), *adv.* In ancient times; of old: *customs observed anciently*. [**ANCIENT** + **-LY**]

ancient Mystic Order Rosae Crucis. See under **Rosicrucian** (def. 2). **Abbr.**: AMORC

ancient of Days, the Supreme Being; God.

ancient of Days, *The*, a hand-colored print by William Blake, the frontispiece of his poem *Europe* (1794).

ancientry (än'shən trē), *n.* 1. *Archaic*. a. ancient character or style. b. ancient times. 2. Obs. a. ancient lineage. b. old people. [**ANCIENT** + **-RY**]

ancile (än sil'ē), *n.* 1. *pl.* an-cil-i-a (än sil'ē a, äng kil'ē). *Rom. Religion*. 1. a shield given by Mars to Numa Pompilius as the palladium of Rome. 2. any of 11 counterfeits of this shield, carried with it on ceremonial occasions. [*L.* equiv. to *an-* (var. of *ambi-*) + *-cile*, akin to *caedere* to cut]

ancilla (än sil'ē), *n.* *pl.* -las. 1. an accessory; auxiliary or adjunct. 2. *Archaic*. a maidservant. [see **ANCILLARY**]

ancillary (än'sə ler'ē or, *esp.* Brit., an sil'ē rē), *adj.* accessory; auxiliary: *an ancillary function*. [*< L. ancillā(-us)* relating to maid-servants, equiv. to *ancillā* (a) maid-servant (*ancilla*) maid-servant + *-illa* dim. suffix] + *-arius* -ARY- (*r.* -ARIS -AR'Y)]

ancipital (än sip'i tēl), *adj.* Bot., Zool. two-edged: *ancipital stems*. [*< L. ancipit-* (s. of *anceps*) two-headed, two-sided (*an-*, var. of *ambi-*) + *-cipit-*, var. of *caput* head] + **-AL-**]

ancus (än'shūs), *n.* *Class. Myth.* a centaur.

anco-hu-ma (äng'kō hō mā), *n.* a peak of Mount Sorata. Cf. **Sorata**, Mount.

ancon (äng'kon), *n.* *pl.* an-con-es (äng'kō nēz). 1. the elbow. 2. *Arch.* a bracket or console, as one supporting part of a cornice. [*< L. < Gk. ankōn* elbow] — **an-con-al** (äng'kō nāl), *adj.* — **an-con-old** (äng'kō nēl), *adj.* — **an-con-old**, *adj.*

ancon (äng'kon; Sp. äñ'kon), *n.* a town in the Canal Zone, near the city of Panama: medical center of the Canal Zone. 1946 (1950).

an-co-na (än kō'nā; Eng. äng'kō'nā), *n.* *pl.* -ne (-ne), Eng. -nas. *Italian*. an altarpiece, usually consisting of a painted panel or panels, reliefs, or statues set in an elaborate frame.

an-co-na (än kō'nā), *n.* 1. a seaport in E Italy, on the Adriatic Sea. 99,678 (1961). 2. one of a Mediterranean breed of chickens having mottled black-and-white plumage.

an-crē (äng'krē), *adj.* *Heraldry*. (of a cross) having the end of each limb divided and carved outward like the flukes of an anchor; moline: *a cross ancrē*. Also, **anchory**. [*< F.* equiv. to *anchre* ANCHOR + *ē* (*< L. -atus* -ATE)]

An-cus Mar-ci-us (äng'kās mār'shūs), *Rom. Legend*. a king of Rome during whose reign the first bridge across the Tiber is believed to have been constructed.

-ancy, a combination of **-ance** and **-y**, used to form nouns denoting state or quality: *brilliance*. [*< L. -antia*, equiv. to *-ā* thematic vowel + *-nt-* prp. suffix + *-ia* -Y]

ancylō-, a learned borrowing from Greek meaning "hook," "joint," used in the formation of technical terms: *ancylotomiasis*. Also, **ancylō-**, **ankylō-**. [*< Gk. ankylō-* (s. of *ankylōs*) crooked, curved, equiv. to *ankōs* bend (*< L. uncus* bent, *E* angle to fish with hook and line) + *-ylos* adjective-forming suffix]

an-cy-lo-sis (än'sē lō'sis), *n.* *Pathol.* hookworm (def. 2). Also, *ankylotomiasis*. [*< NL*, equiv. to *Ancylotoma* (a) genus of hookworms (see **ANCYLO-**, **STOMA**) + *-iasis* -IASIS]

and (and; unstressed and, an), *conj.* 1. (used to connect grammatically coordinate words, phrases, or clauses) with; along with; together with; added to; in addition to; besides; also; moreover: *pens and pencils*. 2. as well as: *nice and warm*. 3. then: *He read for an hour and went to bed*. 4. also, at the same time: *to sleep and dream*. 5. again then again; then once more: *He coughed and coughed*. 6. as opposed to different examples of the same kind: *There are dogs and dogs, some mean, some friendly*. 7. (used to introduce a sentence, implying continuation) also; then: *And he said unto Moses*. 8. (used between two finite verbs): *Try and do it*. 9. *Archaic* or *Dial.* if; and you please. Cf. **an²**. 10. so and so forth, and so on; and others; et cetera: *We discussed traveling, sightseeing, and so forth*. 11. and so on, and more of a similar kind; and further in the same way: *It was a summer filled with parties, picnics, and so on*. — **an²**. 12. an added condition or stipulation: *He accepted the job, no and about it*. 13. Often, *and*, an additional detail or particular: *It was a long story, with many ands*. [ME: OE and, ond; c. OS. OHG. ant, OFris. Goth and, Icel and-; akin to G und, D en Skt anti, etc.]

—Usage. Since **ETC.** is an abbreviation for **ET CETERA** which means "and others," the form **ETC.** is condemned as being redundant. Use **ETC.** or **AND OTHERS** or **AND SO FORTH** instead.

and... *Music* *andante*.

an-da-lu-sia (än'də'loo'shə, -shēə), *n.* a region in Spain, bordering on the Atlantic Ocean and the Mediterranean Sea. 33,712 sq. mi. Spanish. **An-da-lu-si-a** (än'də'loo'shē'ā).

— **An-da-lu-si-an**, *adj.* *n.* **an-da-lu-si-te** (än'də'loo'sit), *n.* *Mineral*. an orthorhombic form of aluminum silicate, Al_2SiO_5 , found in schistose rocks. [named after ANDALUSIA, where it was first found; see **-ITE**]

Andaman (än'də mən), *adj.* 1. Also, **Andaman-ese**, of or pertaining to the Andaman Islands, their inhabitants, or the inhabitants' language. — **Andamanese** (def. 1).

Andaman and Nicobar Islands (än'də bār' / nīk'ə bār'), a centrally administered territory of India, comprising two groups of islands in the E part of the Bay of Bengal, SW of Burma. 63,548 (1961); 3143 sq. mi. **Cap.**: Port Blair.

Andaman-ese (än'də mən'ēz', -nēs), *n.* *pl.* -ese, *adj.* — **Andaman**, **Andaman**, **Andaman** *Is-lander*, a member of a Negrito people of the Andaman Islands. 2. the language of the Andamanese, not known to be related to any other language despite attempts to connect it with Dravidian and with the aboriginal languages of Australia. — **adj.** 3. **Andaman** (def. 1). [**ANDAMAN** + **-ESE**]

Andaman Islands, a group of islands in the E part of the Bay of Bengal, W of the Malay Peninsula. 18,939 (1951); 2508 sq. mi.

Andaman Sea, a part of the Bay of Bengal, E of the Andaman and Nicobar Islands. 30,000 sq. mi.

an-da-men-to (än'də mən'tō; *It.* än'dä men'tō), *n.* *pl.* -tos, *It.* -ta (-tā). *Music*. 1. an extended fugue subject. 2. an episode in a fugue. [*< It.* equiv. to *anda(re)* to walk, proceed + *-mento* -MENT]

an-dan-te (än dan'tē, än dän'tā; *It.* än dän'tō), *adj.* *adv.* *pl.* -tes. *Music*. — **adj.** *adv.* 1. moderately slow and even. — **2.** an *andante* movement or piece. **Abbr.**: *and.* [*< It.* lit., walking (prp. of *andare* to walk); see **-ANT**]

an-dan-ti-no (än'dan tē'nō, än'dän-; *It.* än'dän tē'nō), *adj.* *adv.* *pl.* -nos, *It.* -na (-nā). *Music*. — **adj.** *adv.* 1. slightly faster than *andante*. — **2.** an *andantino* movement or piece. [*< It.* equiv. to *andante* walking + *-ino* dim. suffix]

an-de-an (än dē'an, än'dē-), *adj.* of or like the Andes. [**ANDE** (s) + **-AN**]

Ande'an con-dor. See under **condor** (def. 1).

Ande'an deer, *huemul*.

Andee-na (än dē'nā), *n.* a girl's given name.

And-el (än'del), *n.* a walled plain in the fourth quadrant of the face of the moon: about 19 miles in diameter.

And-lee (än'dlē), *n.* a girl's given name.

And-er-lecht (änd'er lekht), *n.* a city in central Belgium, near Brussels. 93,734 (est. 1959).

And-er-sen (än'dor sən), *n.* Hans Christian (hanz), 1805-75, Danish author, esp. of fairy tales.

And-er-sen Nex-ō (änd'er sən nīk'sō). See **Nexō**, Martin Andersen.

And-er-son (än'dor sən), *n.* 1. Carl David, born 1905, U.S. physicist; discoverer of the positron: Nobel prize 1936. 2. Dame Judith, born 1898, Australian actress in the U.S. 3. Marian, born 1908, U.S. contralto. 4. Maxwell, 1888-1959, U.S. dramatist. 5. Sherwood, 1876-1941, U.S. novelist and short-story writer. 6. a city in central Indiana. 49,061 (1960). 7. a city in NW South Carolina. 41,316 (1960). 8. a town in N California. 4492 (1960).

And-er-son East/ Side, a town in central Indiana. 3778 (1960).

And-er-son-ville (än'dor sən vil), *n.* a village in SW Georgia: site of a Confederate military prison. 263 (1960).

And-es (än'dēz), *n.* (construed as pl.) a mountain range in W South America, extending ab. 4500 mi. from N Colombia and Venezuela S to Cape Horn. Highest peak, Aconcagua, 22,834 ft.

an-de-sine (än'di zēn'), *n.* a mineral, intermediate in the plagioclase feldspar group, having a play of colors and usually found as crystals in igneous rocks. [named after ANDRES; see **-INE**]

an-des-ite (än'di zit'), *n.* a volcanic rock composed essentially of plagioclase feldspar, resembling trachyte in appearance. [named after ANDRES; see **-ITE**] — **an-de-sit-ic** (än'di zit'ik), *adj.*

And-es light-nig, an electrical discharge of the corona type, occurring over mountains when the area is electrically disturbed. Also called *Andes glow*, *Andes lights*.

Andhra Pra-desh (änd'rā prā dāsh'), a state in SE India, formed from portions of Madras and Hyderabad states. 1956. 35,983,447 (1961); 105,963 sq. mi. **Cap.**: Hyderabad.

Andie (än'dē), *n.* a boy's or girl's given name. Also, **Andy**.

And-i-ki-thi-ra (än'dä ki thēr'ā; Gk. änd'kē thēr'ā), *n.* Antikythera.

and-i-ron (än'dē'ron), *n.* one of a pair of metal stands, usually of iron or brass, for supporting logs in a fireplace. [ME *andyr(n)* *< OF* *andier*? *< Gaulish* **andera* heifer (through use of cows' heads as decorations on andirons); -iron by assoc. with **IRON**]

And-i-zhan (än'di zhān'), *n.* a city in E. Uzbekistan, in the SW Soviet Union in Asia. 129,000 (1959).

and/or, used to indicate that either "and" or "or" is appropriate for linking two words, phrases, or the like: *insurance to cover fire and/or theft*.

an-do-ro-ba (än'dä rō'bā), *n.* carapa. [*< Tupi* *< Sp* or *Pg*]

And-or-ra (än'dā'rā -dor'fā; Sp. änd'ā'rā), *n.* a re-



And in the E Pyrenees between France and Spain. Bishop of Urgel. 7000 (est. 1959). 191 sq. mi. **Cap.**: Andorra. French, *Andorre* (än dōr'). — **Andor-ran**, *adj.*

and-, var. of **andro-** before a vowel: **Androecium**.

An-dra-da e Sil-va (än drä'dä e sēl'vā), *n.* *Jo-sé Bo-ni-fa-ci-o-de* (zhō zē' bō'nē fā'syō dō), 1763-1838, Brazilian statesman and scientist.

an-dra-dite (än'drā-dit'), *n.* a mineral, calcium-iron garnet, $Ca_2FeSi_2O_8$, occurring in brown, green, or black crystals. [named after J. B. d'ANDRADE SILVA; see **-ITE**]

An-drās-sy (än dras'sē; Hung. on'drā shē), *n.* 1. Count Julius, 1823-90, Hungarian statesman. 2. his son, Count Julius (Gyula), 1860-1929, Hungarian statesman.

An-drē (än'drē or, for 1, an'drē; for 2 also Fr. än drā'), *n.* 1. John, 1751-80, British major hanged as a spy by the Americans in the Revolutionary War. 2. a boy's given name, French form of **Andrew**.

An-dre-a (än'drē ā, än'-, än drā'ā), *n.* a boy's or girl's given name.

An-dre-a del Sar-to (än drē'ā del sār'tō; *It.* ändrē'ā del sār'tō), *n.* 1. (Andrea Domenico d'Annio di Francesco) 1486-1531, Italian painter. 2. (italics) a dramatic monologue (1855) by Robert Browning.

An-dre-a-nof Is-lands (än'drē an'of; Russ. än'drē-ā'nof), a group of islands in the W part of the Aleutian Islands. 1432 sq. mi.

An-dre-ev (än drē'vā), *n.* Andrei An-dre-ovich (ändrē' än drē'vā vich), born 1895, Russian statesman.

An-drew (än'drēv), *n.* 1. one of the 12 apostles of Jesus. Mark 3:18; John 1:40-42. 2. a boy's given name.

An-dre-wes (än'drēvēs), *n.* Lancelot, 1555-1626, English theologian; one of the translators of the Authorized Version of the Bible.

An-drew of Crete, A.D. 650-730, Greek Orthodox archbishop of Crete; poet; reputed inventor of the musical canon.

An-dre-ws (än'drēvōz), *n.* 1. Charles McLean (mā klān'), 1863-1943, U.S. historian and author. 2. Roy Chapman, 1884-1960, U.S. naturalist, explorer, and author. 3. a town in E South Carolina. 2995 (1960).

An-dre-yev (än drē'yaf), *n.* Le-onid Nī-ko-la-e-ovich (lē o nēd' nī kō lē'yā vich), 1871-1919, Russian novelist, short-story writer, and playwright. Also, **An-dre'ev**.

An-drič (änd'rīch), *n.* I-vo (vō'vō), born 1892, Yugoslavian poet, novelist, and short-story writer: Nobel prize 1961.

An-dri-ette (än'drē et'), *n.* a girl's given name.

andro-, a learned borrowing from Greek meaning "male," used in the formation of compound words: *androsterone*. Also, **andr-**, **-androus**. [*< Gk. andrō(s)*, gen. of *andrō* old man; akin to *Skt. nara-*, *L. Nero*]

an-dro-cent-ric (än'drō sən'trik), *adj.* dominated by males or by masculine interests: *an androcentric society*. [**ANDRO-** + **CENTRIC**]

An-dro-cle-a (än'drō klē'ā), *n.* *Class. Myth.* a daughter of Antipopeus of Thebes. Cf. **Alecia**.

An-dro-cles (än'drō klēz'), *n.* a legendary Roman slave who was spared in the arena by a lion from whose foot he had long before extracted a thorn. Also, **An-dro-cleus** (än'drō klēs).

An-dro-cles and the Lion, a comedy (1913) by G. B. Shaw.

an-dro-clin-i-um (än'drō klin'ē-əm), *n.* *pl.* -clin-i-a (-klin'ē-ā). *Bot.* *clinandrium*. [*< NL*, equiv. to *andro-* + *-clinium* *< Gk. klinion*, dim. of *klinē* bed; see **-CLIN-**]

an-dro-co-ni-um (än'drō kō'nē-əm), *n.* *pl.* -ni-a (-nē-ā). a scale on the forewing of certain male butterflies from which an odor attractive to females is emitted. [*< NL*, equiv. to *andro-* + *-conium* *< Gk. kōnion*, neut. of *kōnios* dusty (*kōnī(s)* dust + *-os* adj. suffix)]

an-dro-cra-cy (än drō'krā sē), *n.* social rule by men. [**ANDRO-** + **-CRACY**] — **an-dro-cra-tic** (än'drō krat'ik), *adj.*

An-dro-cra-tēs (än drō'krā tēz'), *n.* *Class. Myth.* the hero who founded Plataea.

an-dro-di-oe-cious (än'drō dī'ōē'shūs), *adj.* *Bot.* having staminate and monoclinous flowers on separate plants of the same species. [**ANDRO-** + **DIOECIOUS**] — **an-dro-di-oe-cism** (än'drō dī'ōē'siz-əm), *n.*

an-dro-e-ci-um (än drē'shē-əm), *n.* *pl.* -cia (-shē-ā). *Bot.* the stamens of a flower collectively. [*< NL* *< Gk. andrō-* + *-eikion*, dim. of *otkos* house] — **an-dro-e-cial** (än drē'shēl), *adj.*

an-dro-gam-one (än'drō gam'ōn), *n.* *Biochem.* a gamone liberated by a male gamete. [**ANDRO-** + **GAMONE**]

an-dro-gen (än'drō jən), *n.* *Biochem.* any substance, natural or synthetic, that promotes masculine characteristics. [**ANDRO-** + **-GEN**] — **an-dro-gen-ic** (än'drō-jen'ik), *adj.*

An-drog-e-us (än droj'ē-əs), *n.* *Class. Myth.* a son of Minos and Pasiphaë who fell victim to the machinations of Athenian King Aegeus: in revenge for his son's death, Minos waged war on the Athenians and forced them to send a tribute of seven maidens and seven youths to the Minotaur every nine years.

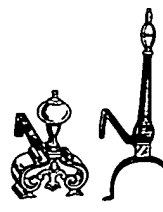
an-dro-gyne (än'drō jīn'), *n.* an androgynous organism. [*< MF* *< L. androgyn(us)* *< Gk. andrōgynos* hermaphrodite, equiv. to *andro-* + *gyn-* GYN- + *-os* masc. n. suffix]

an-drog-y-nous (än droj'ē-nēs), *adj.* 1. *Bot.* having staminate and pistillate flowers in the same inflorescence. 2. being both male and female; hermaphroditic. [**ANDROGYN-** + **-OUS**] — **an-drog-y-n-y**, *n.*

An-drom-a-che (än drom'ā kē'), *n.* 1. *Class. Myth.* the wife of Hector and mother of Astyanax. 2. (italics) a tragedy (c.419 B.C.) by Euripides.

An-dro-ma-cue (än drō mak'f), *n.* a tragedy (1667) by Racine.

An-drom-e-da (än drom'ē dā), *n.* See **Japanese andromeda**. [*French* use of *Andromeda*]



Andirons